REMARKS

This is a full and timely response to the outstanding Supplemental Non-Final Office Action mailed July 9, 2008. Reconsideration and allowance of the application and presently pending claims, as amended, are respectfully requested.

Present Status of Patent Application

Upon entry of this Amendment, claims 1-48 are pending in the present application. Claims 29, 30, and 46-48 are withdrawn from consideration. Claims 1, 25, and 31 are amended herein.

The prior art made of record has been considered, but is not believed to affect the patentability of the presently pending claims. Applicants believe that no new matter has been added and that a new search is not necessary.

The Examiner is thanked for vacating the previous Office Action mailed on March 18, 2008 and for issuing the present Non-Final Office Action as a Supplemental Action. The Examiner is further thanked for considering and examining claims that were inadvertently withdrawn in Applicant's previous correspondence dated January 25, 2008. Also, the Examiner and Examiner's supervisor are thanked for attending the telephonic interview on June 9, 2008 to discuss the above-mentioned inadvertent withdrawal of claims and the art cited in this case.

Claim Objection

Claim 25 was objected to under 35 CFR 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 25 has been amended to depend from claim 13, instead of claim 24, thereby rendering this objection moot.

Double Patenting

A non-statutory double patenting rejection was raised in view of co-pending application 10/861,809. This is a provisional obviousness-type double patent rejection.

Upon allowance of claims in either this application or co-pending application 10/861,809, any issue of double patenting will be addressed at that time.

Claim rejection under 35 U.S.C. §103(a)

Claims 1-28 and 31-45 were rejected under 35 USC §103(a) as being unpatentable over Phillips (US2002/0045646) and Bergstrand (US 5,817,338). Applicants respectfully traverse this rejection.

Claim 1 and claims 2-28 dependent therefrom

Independent claim 1 of the present application is directed to an oral pharmaceutical composition comprising multiple active substrate populations provided in a capsule. Claim 1 as amended herein clearly recites the active substances as comprising "three ***distinct*** populations". The three distinct populations of the active substances in the capsules, as recited in claim 1, are taught in the present specification. See, for example, the specification at page 8, line 21 to page 9, line 11, which reads as follows:

> "The pharmaceutical capsule of the invention is made such that each population of beads, pellets, tablets or granules has a distinct physiological function.
>
> The function of the first population, comprising the pharmaceutically active substance, such as a proton pump inhibitor compound (PPI), that is rapidly releasable, is to deliver the pharmaceutical active beginning in the stomach. This is made possible due to the presence of an optional excipient and by the stable environment created by the elevated pH environment of the stomach brought about by the rapid disintegration and dissolution of the population of basic substance whose function is to rapidly deliver basic material to the stomach, which allows for precise control of the stomach pH to more than about 4.0 and less than about 7.0 and, typically, less than about pH 6.3. This pH can also be achieved in less than about 1 hour.
>
> The function of the second population, comprising the pharmaceutical active substance, such as a proton pump inhibitor compound (PPI), that is released slower than that of the first population, is to deliver another quantity of the pharmaceutical active between the duodenum and just past the ileocecal junction. This is possible due to the presence of an excipient that controls the release of the pharmaceutical active and the choice and quantity of the basic substance delivered in the stomach by the population of basic substance. The pharmaceutical active substance of the second population may be released in a delayed and/or sustained manner."

Further examples of the descriptions of multiple physically distinct populations are provided in the specification of the present application at, for example, page 11, lines 10-32, and throughout the Examples.

To further clarify the distinct feature of specific populations of active substances, as claimed in claim 1, claim 1 has been herein amended to now recite "wherein (i), (ii) and (iii) are three distinct populations."

In contrast to the compositions as claimed in the present application, the cited references of Phillips and Bergstrand, individually or in combination, do not teach, or otherwise suggest, a capsule comprising at least three distinct populations of active substances.

Applicants also note that Example VI of the cited Phillips reference teaches tablets that are compounded using known methods to form an inner core of omeprazole powder mixed with sodium bicarbonate, and an outer core of omeprazole enteric-coated granules mixed with known binders and excipients. Phillips, therefore, teaches that the omeprazole powder and sodium bicarbonate are uniformly mixed together to form a single population. Also, again as described in Example VI of the Phillips reference, the inner core is disbursed in the stomach where it is absorbed for immediate therapeutic effect, while enteric-coated granules are later absorbed in the duodenum. Thus, Example VI of Phillips teaches, at most, two distinct populations and does not describe the "three distinct populations" as claimed in claim 1 of the present application.

Applicants further assert that claim 1 of the present application recites a "capsule". **Bergstrand clearly teaches away from the use of a capsule.** Bergstrand mentions capsule in the context of prior art only, and discusses the **disadvantages** of such prior art capsule at column 2, lines 1 to 11.

Bergstrand further teaches the use of pellets obtained from capsules (see Bergstrand, Examples 1 and 11, at column 18). The disadvantages of the pellets obtained from capsules are shown in Table II at column 19. Specifically, Table II of Bergstrand shows that pellets obtained from the capsules do not show good acid resistance when formulated in a tablet. The entire disclosure of Bergstrand is directed to tablets and teaches away from the use of capsules.

Applicants, therefore, assert that the cited references of Phillips and Bergstand, for at least the above reasons, do not teach, individually or in combination, the encapsulated formulations comprising three distinct active substance populations form as claimed in claim 1 as amended herein, and in claims 2-28 dependent therefrom. Applicants, therefore, respectfully request that this rejection under 35 USC §103(a) be withdrawn.

Claim 31 and claims 32-45 dependent therefrom

Claim 31 is directed to an oral pharmaceutical composition comprising multiple populations provided in a capsule. Claim 31 clearly recites the active substances as comprising "four ***distinct*** populations". The four distinct populations of the active substances in the capsules, as recited in claim 31, are taught in the present specification. See, for example, the specification at page 8, line 21 to page 9, line 11, which reads as follows:

> "The pharmaceutical capsule of the invention is made such that each population of beads, pellets, tablets or granules has a distinct physiological function.
>
> The function of the first population, comprising the pharmaceutically active substance, such as a proton pump inhibitor compound (PPI), that is rapidly releasable, is to deliver the pharmaceutical active beginning in the stomach. This is made possible due to the presence of an optional excipient and by the stable environment created by the elevated pH environment of the stomach brought about by the rapid disintegration and dissolution of the population of basic substance whose function is to rapidly deliver basic material to the stomach, which allows for precise control of the stomach pH to more than about 4.0 and less than about 7.0 and, typically, less than about pH 6.3. This pH can also be achieved in less than about 1 hour.
>
> The function of the second population, comprising the pharmaceutical active substance, such as a proton pump inhibitor compound (PPI), that is released slower than that of the first population, is to deliver another quantity of the pharmaceutical active between the duodenum and just past the ileocecal junction. This is possible due to the presence of an excipient that controls the release of the pharmaceutical active and the choice and quantity of the basic substance delivered in the stomach by the population of basic substance. The pharmaceutical active substance of the second population may be released in a delayed and/or sustained manner."

Further examples of the descriptions of multiple physically distinct populations are provided in the specification of the present application at, for example, page 11, lines 10-32, and throughout the Examples.

To further clarify the distinct feature of specific populations of active substances, as claimed in claim 31, claim 31 has been herein amended to now recite "wherein (i), (ii) and (iii) are four distinct populations."

In contrast to the compositions as claimed in the present application, the cited references of Phillips and Bergstrand, individually or in combination do not teach, or otherwise suggest, a capsule comprising at least four distinct populations of active substances.

Applicants also note that Example VI of the cited Phillips reference teaches tablets that are compounded using known methods to form an inner core of omeprazole powder mixed with sodium bicarbonate, and an outer core of omeprazole enteric-coated granules mixed with known binders and excipients. Phillips, therefore, teaches that the omeprazole powder and sodium bicarbonate are uniformly mixed together to form a single population. Also, again as described in Example VI of the Phillips reference, the inner core is disbursed in the stomach where it is absorbed for immediate therapeutic effect, while enteric-coated granules are later absorbed in the duodenum. Thus, Example VI of Phillips teaches, at most, two distinct populations and does not describe the "four distinct populations" as claimed in claim 31 of the present application.

Applicants further assert that that claim 31 of the present application recites a "capsule". **Bergstrand clearly teaches away from the use of a capsule.** Bergstrand mentions capsule in the context of prior art only, and discusses the **disadvantages** of such prior art capsule at column 2, lines 1 to 11.

Bergstrand further teaches the use of pellets obtained from capsules (see Bergstrand, Examples 1 and 11, at column 18). The disadvantages of the pellets obtained from capsules are shown in Table II at column 19. Specifically, Table II of Bergstrand shows that pellets obtained from the capsules do not show good acid resistance when formulated in a tablet. The entire disclosure of Bergstrand is directed to tablets and teaches away from the use of capsules.

Applicants, therefore, assert that the cited references of Phillips and Bergstand, for at least the above reasons, do not teach, individually or in combination, the encapsulated formulations comprising four distinct active substance populations form as claimed in claim 31 as amended herein, and in claims 32-48 dependent therefrom. Applicants, therefore, respectfully request that this rejection under 35 USC §103(a) be withdrawn.

CONCLUSION

In light of the foregoing amendments and for at least the reasons set forth above, Applicants respectfully submit that all objections and/or rejections have been traversed, rendered moot, and/or accommodated, and that the now pending claims are in condition for allowance. Favorable reconsideration and allowance of the present application and all pending claims are hereby courteously requested.

Any other statements in the Office Action that are not explicitly addressed herein are not intended to be admitted. In addition, any and all findings of inherency are traversed as not having been shown to be necessarily present. Further, any and all findings of well-known art and official notice, or statements interpreted similarly, should not be considered well known for at least the specific and particular reason that the Office Action does not include specific factual findings predicated on sound technical and scientific reasoning to support such conclusions.

If, in the opinion of the Examiner, a telephone conference would expedite the examination of this matter, the Examiner is invited to call the undersigned attorney at (770) 933-9500.

Respectfully submitted,

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